Humber Health Partnership

Protocol Design SOP

Document control use only	
Reference	R&D GCP SOP 02
Directorate / Care Group	Research & Development
Version	Version 4
Result of last review	Updated Regulations
Issue date	30/04/2026

Author / Owner Use Only	
Group or Trust specific document	Humber Health Partnership HHP (Group)
Date approved by owner (for minor changes only outside committee)	N/A
Date approved	13/5/2026
Approving body	Sponsor Oversight Group / RDI Committee
Next full review date	12/05/2029
Lead Director	Professor Sathyapalan – R&D Director James Illingworth – R&D Manager
Document type	Standard Operating Procedure
Author / Contact	Leanne Cox – R&D QA Manager
Key words	GCP, SOPs, R&D, Research & Development

Distribution:	HHP R&D internet Click on GCP SOPs for HHP-sponsored CTIMPs https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

When this document is viewed as a paper copy, the reader is responsible for checking that it is the most recent version.
Printed copies valid only if separately controlled

AI update statement: This Standard Operating Procedure (SOP) was reviewed and updated with the assistance of an Artificial Intelligence (AI) tool. The AI output was used to support drafting and editing only; all content was verified, amended where required, and approved by the document owner/author in accordance with the Trust's document control and governance requirements.

Authorized by		Sign	Date
R&D Director	Professor Thozhukat Sathyapalan	DocuSigned by: 4C017C4E8DDA44B...	13/5/2026
R&D Manager	James Illingworth	DocuSigned by: 3DDA0F96873F430...	13/5/2026

This page details the version history and the main changes made for each new version.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, 16.10.12	J Pacynko & J Illingworth	Original SOP approved by R&D Committee on 15.10.12
Version 2, 23.11.15	J Pacynko	Weblinks up-dated Hyperlinks removed as no longer work New HRA protocol guidance and template used
Version 3, 17.02.21	S Moffat	SOP changed to new format Weblinks updated
Version 4, draft	L Cox	*Section 1* Added new subsection introducing Quality by Design (QbD) principles and the requirement for a risk-proportionate approach to protocol development, in line with ICH E6(R3). *Section 3* Expanded to include requirements for identifying and documenting Critical-to-Quality (CtQ) factors during protocol design. *Section 3* Added new wording in mandating a trial-level risk assessment, including risk mitigation strategies and justification of design decisions. Introduced participant-centred design expectations in *Section 3* including assessment of participant burden, feasibility and inclusivity of eligibility criteria. Added guidance on the consideration and documentation of digital health technologies and decentralised trial elements (e.g., remote visits, telemedicine) within the protocol. *Section 3* Added new requirements in for describing data governance, including data flow, metadata, audit trails, computerised systems validation and data integrity expectations. Added wording on protocol flexibility and adaptability to reduce unnecessary amendments and deviations. *Section 4* Updated to require QA review of QbD elements, CtQ factors, risk assessments, participant burden considerations, data governance and digital/decentralised elements. *Section 5* Updated to include implementation expectations for QbD, risk-based approaches and data governance, including staff training. Expanded *Appendix 1 – Protocol Summary Template* to include new fields for CtQ factors, risk assessment summary, participant burden, digital/remote elements and data governance overview. Format of SOP to align with HHP Group Template.

Please note for definitions of acronyms refer to Appendix 2 of Management of SOPs. Refer to Appendix 3 of Management of SOPs for the standards to which clinical trials that investigate the safety and/or efficacy of a medicinal product are conducted.

All the HHP R&D GCP SOPs are available at:
https://www.hey.nhs.uk/research/researchers/gcp-sops-for-huth-sponsored-ctimps/

1 Introduction, background and purpose

1.1 The protocol is a document that describes the objectives, design, methodology, statistical considerations and organisation of a trial. The protocol usually also gives the background and rationale for the trial (ICH GCP 1.44, UK CT reg 2 (1).

1.2 Every clinical trial requires a protocol which forms a contract between the investigator and Sponsor. It is therefore important that the protocol is signed off by the Chief/Principal Investigator and Sponsor representative (usually the R&D Manager).

1.3 The clinical trial **must be** conducted in accordance with the protocol (UK CT reg 29 (a). The Sponsor needs be alerted straight away if the protocol requires a change or clarification because it is the Sponsor's responsibility to decide whether an amendment is substantial or non-substantial and which approvals are required if the amendment is substantial. See Amendments SOP for details of the process.

1.4 The purpose of this SOP is to describe how the protocol should be prepared for clinical trials sponsored by Hull University Teaching Hospitals NHS Trust.

1.5 The development of a clinical trial protocol should incorporate Quality by Design principles. This includes the prospective identification of factors that are critical to participant safety, rights and well-being, and to the reliability of trial results. Protocol development should include a proportionate, risk-based approach to trial design, ensuring that procedures, data

collection and operational activities are appropriate to the level of risk and do not impose unnecessary burden on participants or investigators.

2 Who should use this SOP

2.1 This SOP should be used by:

- All research staff involved with HPP-sponsored CTIMPs – Chief/Principal Investigator, other study medics, research nurses, project managers, clinical trial co-ordinators, data managers, administrators etc.
- Clinical trials pharmacy staff – technicians and pharmacists.
- All HHP R&D staff.
- Research staff involved with HHP-sponsored non-CTIMPs may find this SOP a useful guide, although the SOP will need to be adapted for the non-CTIMP study.
- Research staff involved with clinical trials sponsored by an external organisation where the Sponsor has no SOP for the protocol. HHP R&D SOPs are defaulted to in this case.

3 Preparation of the protocol

3.1 The Chief/Principal Investigator will submit the protocol along with the Sponsorship Request Form. The Sponsorship Request Form sign posts to HUTH RDI protocol guidance (specific guidance available for CTIMPs and Non-CTIMPs) available on the RDI website. The SRF encourages that the submitted protocol is completed as much as possible at time of sponsorship request. See R&D GCP SOP 05 Sponsorship of HHP CTIMPs for full process.

3.2 The Protocol Summary template in Appendix 1 can be used by investigators to provide an initial draft outline of the protocol. It is also useful to put this summary towards the front of the protocol for a quick reminder of the protocol design.

3.3 Once it is established whether the study is a CTIMP or non-CTIMP, R&D will send to the Chief/Principal Investigator the CTIMP or non-CTIMP protocol guidance and template for HUTH-sponsored trials in order to finalize the protocol. **These are available from the HHP R&D QA team.**

3.4 The protocol guides are intended to help researchers with points to consider for the content of protocols. The guides indicate the information that should be included in a protocol and cover methodology considerations and requirements specified under Good Clinical Practice (ICH GCP section 6).

3.5 Each section of the protocol guide should be considered carefully. **It is a condition of sponsorship that the protocol guides are adhered to and it is the expected standard for Trust R&D approval.**

3.6 During protocol development, the Chief/Principal Investigator must identify and document the Critical-to-Quality (CtQ) factors relevant to the proposed trial. CtQ factors are those aspects of the trial that are essential to protecting participants and ensuring the reliability and interpretability of trial results. These factors should be explicitly considered when designing study procedures, visit schedules, data collection requirements and monitoring strategies.

3.7 A proportionate, trial-level risk assessment should be undertaken during protocol development. This assessment should identify foreseeable risks to participants and risks to the integrity of critical data. The protocol should describe the strategies implemented to minimise, monitor and mitigate these risks. Risk mitigation measures should be proportionate to the importance of the data being collected and the level of risk associated with trial participation.

3.8 The CTIMP protocol guide and template has been taken from the Health Research Authority (HRA) website - see link below. We have added to this guide wording in red font which is specific for HUTH-sponsored CTIMPs and which should be cut and pasted into the protocol. The red wording has been developed to ensure compliance with the UK CT Regs and ICH GCP, but where it does not reflect the investigator's practice the wording should be revised accordingly.

3.9 Protocol design should consider participant perspectives and aim to minimise unnecessary burden. This includes evaluating the number and frequency of study visits, the volume of procedures, travel requirements, and the overall feasibility of participation. Where appropriate, the protocol should justify the inclusion or exclusion of specific participant groups to support diversity and representativeness of the population intended to benefit from the investigational product.

3.10 Using the HRA's protocol guide will prevent queries raised by the Ethics Committee and MHRA and delays obtaining approvals. https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/

3.11As part of trial set-up, investigators will need to read the R&D GCP SOPs (standard operating procedures) to be aware of their responsibilities as investigators. These SOPs are instructions on how to set up and conduct HUTH-sponsored CTIMPs and are available on the HUTH R&D GCP SOPs webpage at: https://www.hey.nhs.uk/research/researchers/gcp-sops-for-huth-sponsored-ctimps/

3.12 The protocol, patient information sheet, consent form, GP letter and CRF must have a version number and date within the header or footer. See the R&D GCP SOP 01 – Version Control.

3.13 Where appropriate, the protocol should consider the use of digital health technologies (e.g., wearables, sensors, electronic patient-reported outcomes) and decentralised trial elements such as remote visits, telemedicine, or home-based procedures. The protocol should describe the rationale for their use, the procedures for data capture and management, and any associated risks or limitations. These technologies should be selected and implemented in a manner that is appropriate for the participant population and trial objectives.

3.14 It is advisable that investigators contact a statistician in the early stages of developing their protocol. Current guidance or signposting to potential statistical support will be available on the RDI website.

3.15 The protocol should outline the data governance approach for the trial, including data flow, data capture methods, metadata requirements, audit trails, and procedures for data review, correction and finalisation. Where computerised systems are used, the protocol should reference system validation, user access controls, data security measures and contingency plans for system failure.

Where appropriate, the protocol should incorporate pre-specified flexibility or adaptive elements to reduce the likelihood of avoidable amendments and protocol deviations.

Any adaptive features should be clearly described, including the conditions under which adaptations may occur and the procedures for documenting and implementing such changes.

3.16 As a minimum, the Chief/Principal Investigator, Sponsor and Statistician (if involved) should sign off the protocol. The Chief/Principal Investigator signs to agree to conduct the study according to the protocol, the Sponsor representative signs to confirm that Hull University Teaching Hospitals NHS Trust agrees to sponsor the study and the Statistician signs to confirm that the statistics section is correct.

3.17 It is highly recommended that the protocol contains a schedule of assessments in the form of a table with study visits along the top row and investigations/procedures down the left hand column. It is then clear at a glance what study investigations are performed at which visit. This is a good training tool for those involved with the study. An example table is in Appendix 4 at the end of the HRA protocol guide.

3.18 Likewise it is recommended that a flow chart or schematic diagram of the trial design and procedures is present in the protocol which at a glance shows the treatment options and the patients' possible pathways along the study.

3.19 If the study is a randomized controlled trial, it is recommended that the CONSORT website is consulted when compiling the protocol (Consolidated Standards of Reporting Trials http://www.consort-statement.org/).

4 Review of the protocol

4.1The Chief/Principal Investigator will be asked to send the final draft protocol and sponsorship request form to the QA Manager or Monitor for review and decision on sponsorship. Any comments regarding the protocol will be sent back to the investigator for resolving. This helps prevent modifications to the protocol and submission of an amendment after the study has started. See R&D GCP SOP 05 Sponsorship of HHP CTIMPs.

4.2 As part of the sponsorship review, the QA Manager or Monitor will confirm that the protocol adequately addresses Quality by Design principles, identification of Critical-to-Quality factors, risk assessment and mitigation strategies, participant burden considerations, data governance requirements and the use of digital or decentralised trial elements where applicable. Any deficiencies identified during review must be resolved prior to sponsorship approval.

5 Implementation

5.1Implementation of this SOP will conform to the process outlined in R&D SOP 01Management of SOPs. Implementation of this SOP requires investigators and research teams to ensure that Quality by Design principles, risk-based approaches, participant-centred considerations and data governance requirements described in the protocol are operationalised during trial conduct. Training should be provided to all relevant staff to ensure understanding of these elements and their application in practice.

Appendix 1
Protocol Summary

Title	
Chief/Principal Investigator	
Planned sponsor	
Planned funder	
Background	
Phase	1, 2, 3 or 4
Planned number of sites	
Critical-to- Quality Factors	
Design	Number of arms, randomised, placebo-controlled, open label, single-blind, double-blind, parallel design, cross-over.
Aims	
Primary objectives	
Secondary objectives	
Risk Assessment Summary	
Population	
Participant Burden Considerations	
Target accrual	
Duration patient in trial	Duration in treatment phase: Duration in follow-up:
Inclusion criteria	
Exclusion criteria	
Digital or Remote Trial Elements	
Randomisation	
Trial treatment	
Investigations	
Definition of end of trial	
Statistical summary	
Data Governance Overview	